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Clinical Study

Development of a scoring system for predicting adjacent vertebral fracture after balloon kyphoplasty

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ABSTRACT

BACKGROUND CONTEXT: The incidence of adjacent vertebral fracture (AVFs) is reported to be 10%−38% after balloon kyphoplasty. However, no reports have established a system for prediction of AVF occurrence.

PURPOSE: To establish a scoring system for predicting AVF occurrence after balloon kyphoplasty for osteoporotic vertebral fractures (OVFs).

DESIGN: A prospective cohort study.

PATIENT SAMPLE: Consecutive elderly patients aged 65 years and older who underwent balloon kyphoplasty for OVFs within 2 months after the onset.

OUTCOME MEASURES: AVF was confirmed by X-ray.

METHODS: From 2015 to 2017, 116 consecutive patients from 10 participating hospitals who underwent balloon kyphoplasty were enrolled in this study. Prior to study enrollment, each patient underwent plain X-ray, computed tomography (CT), and magnetic resonance imaging (MRI) of the thoracic and lumbar spine. Severity of pain was subjectively assessed using a visual analog scale (VAS) based on the average level of back pain that the patient had experienced in the preceding week. After enrollment, subjects underwent balloon kyphoplasty. Quality of life was evaluated using SF-36. Patients were followed up for at least 6 months.

RESULTS: Of the 116 patients enrolled, 109 patients with all the required data at the time of enrolment and the 6-month follow-up were included in the study. A total of 32 patients (29%)

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showed AVFs within the 6-month follow-up. No significant differences were observed in each clinical outcome at 6-month follow-up, although higher VAS score for back pain at 1-month follow-up was observed in the AVF group (37.5) than in the non-AVF group (20.8, p<.001). Wedge angle of vertebrae before surgery was greater in the AVF group (21.6°) than in the non-AVF group (15.7°, p<.001). The change in wedge angle between pre- and postsurgery was greater in the AVF group than in the non-AVF group, whereas the change in local kyphosis was not significantly different. The multiple logistic regression model showed increased odds ratio (OR) of thoracic or thoracolumbar spine, old OVF presence, >25° kyphosis before surgery, and >10°correction for AVF. Based on this result, a simple scoring system for predicting AVF occurrence was developed. The total AVF score was calculated as the sum of the individual scores, which varied from 0 to 6. All patients with 5−6 points sustained AVF.

CONCLUSIONS: More severe wedge angle before surgery, correction degree, old OVF presence, and thoracolumbar level were predictive factors for AVF. All patients with AVF risk score of 5 or more showed AVF. This information may aid preoperative risk assessment, informed shared decision-making, and consideration of potential alternative management strategies.

Keywords: Adjacent vertebral fracture; Balloon kyphoplasty; Osteoporosis, Vertebral fracture, Kyphosis, Scoring system

Introduction

Osteoporotic vertebral fracture (OVF) is a common condition in the elderly and constitutes an important public health concern. Only about one-third of OVF patients seek medical attention, suggesting that most patients are either asymptomatic or have tolerable symptoms [1]. However, in some patients, OVFs cause functional deterioration, severe pain, and limited mobility because of deformity and intractable back pain after the conservative treatment [2]. Balloon kyphoplasty is widely performed as a surgical intervention for OVF, and its effects have been investigated in many previous studies [3−5]. Generally, major complications occur in less than 1% of patients treated for OVFs [6]. However, this procedure has several potential complications, including extrusion of the cement in the spinal canal, subsequent spinal cord injury, infection, hematoma formation, pulmonary embolus, failure to relieve pain, osteomyelitis, and adjacent vertebral fractures (AVFs) [7]. In particular, the incidence of AVFs is relatively high with the rate ranging from 10% to 38% after balloon kyphoplasty or vertebroplasty [7−16]. The majority of AVFs occurred within 2 months after the procedure [17]. Vertebral bodies treated with polymethylmethacrylate cement (PMMA) are stiffer than the fractured vertebra [18], which may consequently transfer greater load to adjacent vertebral levels [19]. Moreover, the influence of AVFs on clinical outcome still remains unclear.

Bone mineral density (BMD), intraosseus cleft, cement leakage, and cement volume have been reported as risk factors of AVFs after vertebroplasty [9,11,13,15]. However, only a few studies elucidated the risk factors of AVF after balloon kyphoplasty [7,16]. Unlike vertebroplasty, balloon kyphoplasty aims not only to secure fracture stabilization, but also to reconstruct the vertebral anatomy and correct the kyphotic spinal deformity. Thus, the purpose of this study was to reveal the risk factors of AVF after balloon kyphoplasty for the treatment of OVF and to establish a scoring system for the prediction of AVF.

Methods

Patients

This prospective cohort study included 116 consecutive patients from 10 participating hospitals who underwent balloon kyphoplasty from 2015 to 2017. Each of the hospitals involved specialized in the management of spinal trauma and spinal cord injury. All patients aged 65 years or older who were referred for back pain were asked to complete a questionnaire about the presence, severity, and duration of pain. Inclusion criteria were OVFs with instability on lateral radiographs in the supine position, visual analog scale (VAS) pain score of 4 or more, and decreased bone density (T scores − 1). In addition, high intensity (similar to cerebrospinal fluid) or diffuse low intensity areas on T2-weighted magnetic resonance imaging (MRI) within 1 month after pain onset was an inclusion criterion in patients who underwent kyphoplasty within the previous 2 months. A previous study [19] showed that MRI findings were associated with delayed union and intractable back pain (sensitivity 93% and specificity 71%). Exclusion criteria were neurological deficits, pathological fracture, suspected underlying malignant disease, and dementia due to the unreliability of clinical outcome. Study eligibility was determined after initial clinical and radiographic evaluation. The study protocol was approved by the institutional review board of each participating hospital. Informed consent was obtained from the patients prior to study participation.

Prior to study enrollment, each patient underwent plain X-ray, computed tomography (CT), and MRI of the thoracic and lumbar spine. Severity of pain was subjectively assessed by the patient using the VAS, based on the average level of back pain that the patient had experienced in the preceding week. Duration of pain before kyphoplasty was used as a surrogate measure for the age of OVFs. Quality of life was evaluated using the SF-36. After the initial clinical and radiographic evaluation, study eligibility was determined. After enrollment, subjects underwent balloon kyphoplasty. Decisions on surgical timing were dependent on the time elapsed since injury on arrival at the hospital, the time required to obtain diagnostic investigations, and the discretion of the attending spinal surgeon. Apart from surgical management, all patients received appropriate medical support including nonsteroidal anti-inflammatory drugs and osteoporosis treatment including daily or weekly teriparatide and other drugs (bisphosphonate, denosumab, and selective estrogen modulators). Lastly, all patients participated in a postoperative rehabilitation regimen and were followed-up for 6 months.

Surgical intervention

Balloon kyphoplasty was performed using Kyphon, Inc. (manufactured by Medtronic Spine LLC, Sunnyvale, CA, USA) under general anesthesia [20]. Patients were positioned prone on a four-poster frame without an excessive reduction of the kyphosis. A deflated balloon was inserted into the vertebral body under a bilateral transpedicular approach and inflated to restore the height of the collapsed vertebral body to its normal position and create an internal cavity under manometric control (a maximum of 400 psi). The balloon was then deflated and withdrawn. The remaining cavity was filled under low pressure with PMMA until the PMMA reached two-thirds of the way back to the posterior vertebral cortex on the lateral fluoroscopic view. After surgery, patients with fractures in the lumbar spine were instructed to wear a tailor-made corset when out of bed. Physical therapy was started to facilitate ambulation on postoperative day 1 with tailor-made hard or soft corset.

Basically, AVFs were conservatively treated using a tailor-made corset. However, revision surgery was performed in patients with uncontrolled back pain after balloon kyphoplasty owing to the instability of the fractured vertebrae, cement migration, and recollapse of the vertebra with or without AVFs.

Image assessment

Plain X-rays were assessed based on lateral views between the supine and weight-bearing positions before surgery, immediately after surgery, and 1, 3, and 6 months postoperatively [17]. Wedge angle of the collapsed vertebral bodies and local kyphosis between superior endplate of upper vertebral bodies and inferior lower vertebral bodies were measured (Fig. 1). Relative height of the anterior wall was calculated using the following formula: [2×affected vertebral height/(lower vertebral height+upper vertebral height)]×100 (Fig. 2) [21]. The fractured site was classified as follows: thoracic spine (T7-10); thoracolumbar spine (T11-L2); and lower lumbar spine (L3-L5).

Cement leakage was defined as the presence of cement extending beyond the posterior wall and was assessed independently on routine direct postoperative CT of the treated levels. Adjacent vertebral deformity was defined as morphometric change including fracture in an adjacent vertebral body after balloon kyphoplasty. The results of AVFs were discussed between two authors until agreement was obtained.

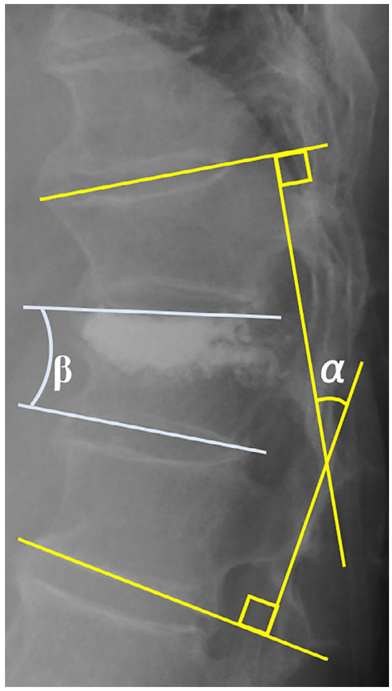

Fig. 1. The local kyphosis including the upper and lower units=α degree. The wedge angle of the vertebral body=β degree.

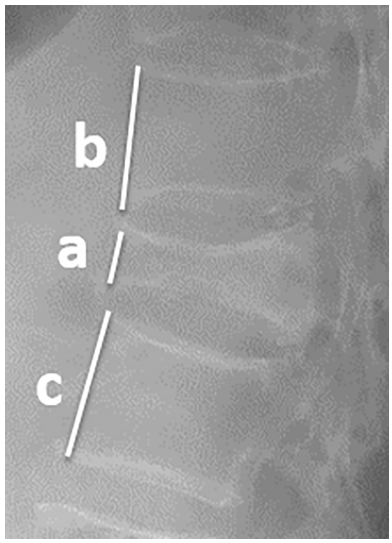

Fig. 2. Percentage height of the anterior wall as calculated by the following formula: [2a/(b+c)]×100.

Statistics

The receiver operating characteristic curve was used to investigate the area under curve of the difference of relative vertebral height and local kyphosis of the fractured vertebrae between pre- and postballoon kyphoplasty for AVFs. Odds ratio (OR) of each variable for AVF was calculated using a logistic regression model adjusted by age, gender, site of fracture (thoracic/thoracolumbar spine and lower lumbar spine), cement volume (mL,) the presence of old OVF, wedge angle before surgery (<20°/20°−25°/>25°), and >10° of correction. Regarding the site of fracture, thoracic spine and thoracolumbar spine were combined into one category, because both AVF and non-AVF groups had only one patient with thoracic fracture. Selection of independent predictors for inclusion in the AVF risk score was based on their relative prognostic contribution in the logistic regression model. For each patient, the AVF risk score was calculated as the simple arithmetic sum of point values assigned to each risk factor based on the multivariate-adjusted risk relationship: 1 point for OR 1.0−10 and 2 points for OR>10. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value of each score for AVF were calculated.

The χ^2 test or Fisher's exact test was used for categorical variables, whereas the *t* test was used for continuous variables. When comparing the change of clinical outcomes between pre- and postballoon kyphoplasty, analysis of covariance was used to adjust for covariates that included each preoperative value. To assess intraobserver and interobserver reliabilities of AVF evaluation on X-ray images, weighted kappa was calculated in 30 randomly chosen vertebral bodies.

Statistical test results were considered significant at p<.05. All p values were two-sided. All analyses were performed using SAS version 9.4 software (SAS Institute, Cary, NC, USA).

Results

Of the 116 patients enrolled, 109 patients with all the required data at the time of enrolment and the 6-month follow-up were included in the present study. With respect to the reliability of AVF evaluation, the weighted kappa showed excellent interrater and intrarater agreement (0.933 and 0.733, respectively).

A total of 32 patients (29%) showed AVFs until 6-month follow-up. Baseline characteristics of AVF and non-AVF groups are shown in Table 1. Mean age was 79.3 years in both groups (p=.957). The proportions of sex, site of injury, BMD, steroid use, and smoking status were also comparable in both groups. However, old OVFs and the use of teriparatide were more frequently observed in the AVF group (p=.053 and p=.059, respectively).

Regarding postoperative complications, cement leakage displayed similar results between the AVF and non-AVF groups (Table 2). The rate of reoperation tended to be higher in the AVF group than in the non-AVF group (p=.075). Posterior fusion was performed in three patients and anterior and posterior fusion was performed in one patient as a revision surgery. The other patients with AVFs (29 patients) underwent conservative treatment. The baseline and final values of SF-36, and VAS scores are shown in Table 2. No significant difference was observed in both SF-36 MCS and PCS at the baseline and 6-month follow-up. Higher VAS score for back

Table 1
Comparison of demographic data between patients with and without adjacent vertebral fracture

	AVF (+) n=32 n (%) or mean (SD)	AVF (−) n=77 n (%) or mean (SD)	p value*
Age, y	79.3 (5.1)	79.3 (5.6)	.957
Sex, female	26 (81%)	61 (79%)	.810
BMI, kg/m^2	21.5 (2.7)	22.4 (3.7)	.212
Level			
Thoracic spine	1 (3%)	1 (1%)	.161
Thoracolumbar spine	30 (94%)	64 (83%)	
Lumbar spine	1 (3%)	12 (15%)	
BMD, g/cm^2	0.657 (0.239)	0.593 (0.253)	.288
Old vertebral fracture			
0	12 (38%)	45 (58%)	.053
≥1	20 (62%)	32 (42%)	
Steroid use, yes	4/31 (13%)	6/70 (9%)	.501
Smoke status			
Nonsmoker	24 (75%)	55 (71%)	1
Former	7 (22%)	18 (23%)	
Smoker	1 (3%)	4 (5%)	
Teriparatide use, yes	15/25 (60%)	23/61 (38%)	.059
Duration to AVF, months	2.0 (1.1)		

BMI, body mass index; BMD, bone mineral density.

* p values were calculated by *t* test for continuous variables and chi-square or Fisher's exact test for categorical variables.

Table 2
Comparison of surgical complications and clinical data before and after surgery between patients with and without adjacent vertebral fracture

	AVF (+) n=32 n (%) or mean (SD)	AVF (−) n=77 n (%) or mean (SD)	p value
Reoperation	3 (9%)	1 (1%)	.075
Cement leak	2 (5%)	12 (17%)	.133
SF-36 PCS			
Preop	5.3 (14.5)	7.9 (16.4)	.430
6-month postop	23.4 (18.7)	26.8 (17.4)	.493
Change	17.4 (19.2)	18.4 (20.1)	.584
SF-36 MCS			
Preop	37.7 (10.2)	38.6 (12.5)	.593
6-month postop	49.2 (9.2)	51.3 (10.1)	.403
Change	10.0 (17.2)	11.8 (16.8)	.503
VAS			
Preop	75.6 (23.8)	72.1 (26.5)	.523
1-month postop	36.4 (23.8)	22.2 (20.0)	.003
3-month postop	28.8 (19.9)	22.2 (21.0)	.183
6-month postop	36.3 (28.7)	27.1 (22.9)	.084
Change	40.8 (39.4)	44.9 (32.2)	.095

AVF, adjacent vertebral fracture; PPV, positive predictive value; NPV, negative predictive value; SF, short-form; PCS, physical component summary; MCS, mental component summary; and VAS, visual analog scale.

pain at 1-month follow-up was seen in the AVF group (36.4) than in the non-AVF group (22.2, p=.003). VAS score at 6-month follow-up tended to be higher in the AVF group than in the non-AVF group (p=.084).

Table 3 shows the results of radiological measurements before and after surgery between the AVF and non-AVF groups. Wedge angle of vertebrae before surgery was greater in the AVF group (21.6°) than in the non-AVF group (15.7°, p<.001). Additionally, relative anterior vertebral height before surgery was shorter in the AVF group (37.3 %) than in the non-AVF group (55.6%, p<.001). Local kyphosis tended to be greater in the AVF group (26.3°) than in the non-AVF group (18.9°, p=.095). The change of wedge angle and relative anterior vertebral height between pre- and postsurgery was greater in the AVF group than in the non-AVF group (10.2° vs. 3.5°, p<.001 and 27.6% vs. 9.7%, p<.001, respectively), whereas the change in local kyphosis displayed no significant difference. Cement volume was greater in the AVF group (5.9 mL) than in the non-AVF group (5.2 mL, p<.046).

Assessed by the area under curve, local kyphosis showed a stronger relationship with AVF than relative vertebral height (Fig. 3). When all of the candidate variables were assessed simultaneously in multivariate analysis, four remained significant predictors of AVF (Table 4). The multiple logistic regression model showed increased OR of thoracic or thoracolumbar spine, old OVF presence, >25° kyphosis before surgery, and >10° correction for AVF. Based on this result, a simple scoring system for predicting

Table 3
Comparison of radiological measurements before and after surgery between patients with and without adjacent vertebral fracture

	AVF (+) n=32 n (%) or mean (SD)	AVF (−) n=77 n (%) or mean (SD)	p value
Wedge angle, degrees			
Preop	21.6 (6.4)	15.7 (6.6)	<.001
<20°	12 (38%)	57 (74%)	
20°−25°	11 (34%)	12 (16%)	
25°−	9 (28%)	8 (10%)	.001
1-week postop	10.0 (6.5)	8.5 (5.9)	.301
6-month postop	11.3 (6.7)	12.4 (5.7)	.359
Change	10.2 (5.9)	3.5 (5.1)	<.001
Local kyphosis, degrees			
Preop	26.3 (12.0)	18.9 (18.1)	.095
1-week postop	19.2 (15.4)	11.8 (11.3)	.045
6-month postop	27.9 (14.7)	19.5 (17.2)	.087
Change	−3.2 (9.1)	−0.5 (6.3)	.271
Relative anterior height, %			
Preop	37.3 (19.1)	55.6 (17.2)	<.001
1-week postop	71.6 (18.5)	78.3 (16.1)	.088
6-month postop	65.7 (14.8)	64.6 (12.7)	.686
Change	27.6 (21.3)	9.7 (5.6)	<.001
Cement volume, mL	5.9 (2.1)	5.2 (1.6)	.046

AVF, adjacent vertebral fracture.

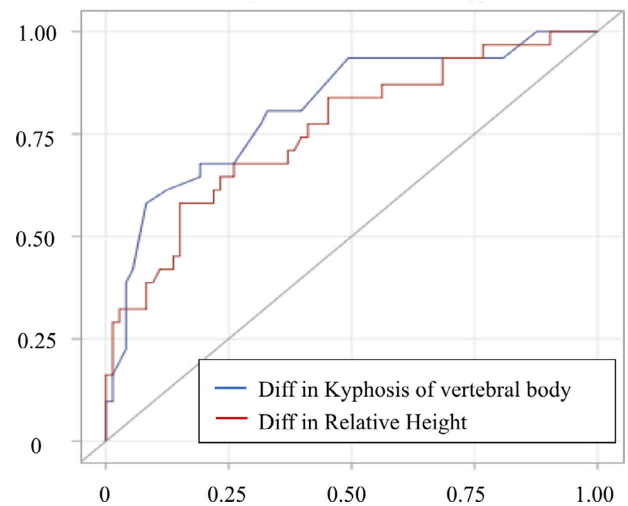

Fig. 3. Area under curve of difference in kyphosis and relative height is 0.814 and 0.759 (p=.167), respectively.

Table 4
Adjusted odds ratio (OR) and scoring for adjacent vertebral fracture

Logistic model	Odds ratio (OR)	Score (1, OR 1−10; 2, OR >10)
Thoracic/thoracolumbar spine	19.9 (1.5−261.0)	2
Cement volume (per mL)	1.1 (0.8−1.6)	0
Old OVF presence	3.7 (1.6−8.7)	1
Wedge angle before surgery		
20°−25°	1.0 (0.2−5.2)	0
25°−	8.4 (1.5−47.7)	1
Correction>10°	12.4 (3.4−46.2)	2

OVF, osteoporotic vertebral fracture.

Table 5
AVF incidence by AVF risk score

Score	AVF+ n=32	AVF− n=77	SEN	SPE	PPV	NPV	Predicted OR
0	0 (0)	2 (3%)					
1	0 (0)	7 (9%)	100	2.6	29.9	100	NA
2	1 (3%)	33 (43%)	100	11.7	32	100	NA
3	13 (41%)	28 (36%)	96.9	45.5	47	97.7	37.2 (4.8−286.4)
4	2 (6%)	7 (9%)	56.3	90.9	72	83.3	12.9 (4.5−36.5)
5	13 (41%)	0 (0)	50	100	100	82.8	NA
6	3 (9%)	0 (0)	9.4	100	100	72.6	NA

AVF, adjacent vertebral fracture; SEN, sensitivity; SPE, specificity; PPV, positive predictive value; NPV, negative predictive value; OR, odds ratio; and NA, not available.

AVF was determined. The total AVF score was calculated as the sum of the individual scores and varied from 0 to 6. Thoracic or thoracolumbar spine was scored 2 points, the presence of old OVF scored 1 point, wedge angle before surgery (>25°) scored 1 point, and >10° of correction scored 2 points.

Sensitivity, specificity, PPV, and negative predictive value were calculated by AVF risk score in the same dataset (Table 5). If the score was 0−1 point, there was no incidence of AVF. PPV was 32% at 2 points, 47% at 3 points, and 72% at 4 points. All patients with 5−6 points showed AVF.

Discussion

This study is the first to demonstrate a scoring system for the prediction of AVF. AVF is reported as one of the causes of revision surgery after vertebroplasty or balloon kyphoplasty [22,23], similar to the results of the current study showing the tendency of increased risk for revision surgery. In addition, VAS score at 6-month follow-up tended to be higher in AVF group. Therefore, it is important to predict the AVF occurrence before performing the procedures.

Pradhan et al. [24] revealed that kyphoplasty reduced vertebral kyphotic deformity at the fractured vertebrae by an average of 7.3° (63% of preoperative kyphosis) as reported by several previous studies [25,26]. However, the correction after kyphoplasty should be considered in the area including the upper and lower spinal segments. Regarding radiological outcome in the current study, patients with AVFs showed greater correction of vertebral body at 6-month follow-up than those without AVFs (10.2° vs. 3.5°, respectively). On the other hand, the correction of local kyphosis was similar in both groups (3.2° vs. −0.5°, respectively), indicating that if the correction was achieved by kyphoplasty, the correction loss would occur according to AVF or correction loss of the vertebral body. When considering the radiological effect, we have to evaluate not only kyphosis of the vertebral body but also segmental kyphosis including the upper and lower segments. However, there have been no reports comparing the image findings including upper and lower segments between the AVF and non-AVF groups. Correction >10° was an independent risk factor for AVF. Therefore, less correction might reduce the risk in patients with a score of 3−4 points before surgery. If the AVF risk score is 5 or more and the goal of surgery is to improve kyphosis of >10°, anterior or posterior fusion surgery with implantation can be one of the options. A further study involving other population cohorts is needed to validate our findings.

Minor cement leakage was frequently noted on CT, but such leakage was asymptomatic in most cases [4]. The amount of injected cement and the restoration of vertebral height by kyphoplasty could have an influence on the long-term outcomes of the procedure. However, these associations have not been demonstrated clinically [27]. Smaller volumes of cement have been shown to decrease the risk of new OVF formation while maintaining sufficient stability [28]. Syed et al. revealed that subsequent AVF and non-AVF after vertebroplasty occurred at roughly equal frequencies in the cement leakage and noncement leakage groups [29]. However, cement leakage is reported as a primary risk factor of new vertebral compression fractures [15,30]. Lin et al. [15] mentioned that hard cement might result in an increased mechanical pressure, eventually causing a new fracture of the endplate in the adjacent vertebral body. Moreover, Takahara et al. [11] mentioned that cement leakage itself does not lead to OVFs. Rather, increased disc stiffness after leakage might have increased the risk of adjacent compression fracture. Hulme et al. [31] concluded that if the cement is not in close contact with the endplates then it does not increase endplate deformation in the adjacent vertebrae, thereby minimizing the risk of AVF. However, Civelek et al. [16] reported that 11/171 (6%) patients who experienced cement leakage into the upper or lower disk spaces after balloon kyphoplasty did not have AVF, whereas in the patients with AVF, there was no cement leakage into the disk spaces. The current study also showed no relationship of cement leakage with AVFs.

Several papers [9,11,29] revealed that decreased BMD scores indicated a risk of AVF following vertebroplasty. Takahara et al. [11] demonstrated that the patients with whom leakage was found had significantly lower BMD scores than the remainder of the cohort. This might suggest that decreased BMD is also a serious risk factor with respect to cement leakage. In comparison to vertebroplasty, kyphoplasty has a potential advantage in the ability to partially reestablish vertebral height, thereby restoring stability of the spine [33]. Therefore, the mechanism of AVFs might be different between the two procedures. Indeed, the current study showed a strong association of the compression severity and surgical correction with AVFs, while there was no difference in the BMD between the AVF and non-AVF groups in the current study. Civelek et al. demonstrated that the two factors identified as being significantly associated with AVFs after balloon kyphoplasty were the sex (p=.001) of the patient and the preoperative wedge angle (p=.013). The patients with new symptomatic compression fracture had higher initial wedge angle than those without fractures. The female group had a higher risk of having new vertebral fractures than the male group. The severity of the osteoporosis (low BMD) was not a determinant in the occurrence of AVFs after balloon kyphoplasty.

Su et al.'s [10] retrospective study demonstrated that the therapeutic effects of teriparatide were better than those of the combined vertebroplasty and an antiresorptive agent in fracture prevention, BMD change, and sustained pain relief. The current study was unable to determine the effect of teriparatide, which might reflect the selection bias of patients who required the therapy. However, considering that most of the AVFs occur within a few months and the effect of increasing BMD appeared at least 3 months after the start of teriparatide use [32], teriparatide should be administered at least before surgery.

This study demonstrated that the incidence ratio of AVF after balloon kyphoplasty was 29%, which is comparable or a little higher compared with previous reports [7−16]. Patients with clefts are at increased risk of subsequent fractures, and treatment of these clefts is associated with increased rates of AVFs [33]. All OVFs had instability in the current study, which might have affected the increase in the incidence of AVFs.

This study has some limitations. The study did not show an apparent impact of AVFs on the clinical outcome, except for back pain at 1-month follow-up. However, Takahara et al. [11] showed a higher incidence of back pain in the AVF group than in the non-AVF group at 1-year follow-up. Furthermore, the follow-up period might be too short to evaluate the clinical outcome. However, since most of the AVFs occurred within the few months, as previously reported [17], this short-term study should be valid to investigate the predicting factors for AVFs.

In conclusion, more severe wedge angle before surgery, correction degree, presence of old OVF, and thoracolumbar level were predictive factors of AVF. All patients with AVF risk score 5 or more showed AVF. Therefore, these patients may benefit from preoperative risk assessment, informed shared decision-making, and consideration of potential alternative management strategies.

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